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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
DAVIS, MINH TAM B	
ART UNIT	**PAPER NUMBER**
1642	37

DATE MAILED: 05/21/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

[illegible]

Office Action Summary	Application No.	Applicant(s)	
	09/030,605	CIUFFO ET AL.	
	Examiner	Art Unit	
	MINH-TAM DAVIS	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 March 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *23,24,29-36 and 41-46* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23,24,29-36 and 41-46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *36* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

The request filed on 03/05/03 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No:09/030606 is acceptable and a CPA has been established. An action on the CPA follows

Accordingly, claims 23-24, 29-36, 41-46 are being examined.

The following are the remaining rejections.

OK cancel dr

REJECTION UNDER 35 USC 101, UTILITY

Rejection under 35 USC 101 of claims 29-34, 41-46 pertaining to lack of specific and substantial or well established utility remains for reasons already of record in paper Nos. 30, 33.

Applicant argues in paper No: 32 that it is more likely than not than one could practice the claimed invention. Applicant argues that Applicant does not claim a method for distinguishing between localized and advanced for metastasized prostate carcinoma. Applicant asserts that as prostate specific markers are not detectable in serum of normal individuals, the identification of the presence of a prostate specific marker in the circulation of a patient is indicative of the presence of prostate cancer in the patient. This utility would be also useful for distinguishing between localized and advanced or metastasized protate carcinoma. Applicant asserts that Gelmini et al supports the claim invention, because Gelmini et al teach that using a new polymerase chain reaction, 32%

of peripheral blood samples form prostate cancer patients are positive, whereas no positive samples are found in the control, healthy subjects.

Applicant further asserts that the disclosure of Gelmini et al, Kibel et al and Ren et al, which teach that it is unpredictable that metastasized prostate cells still express the claimed sequence, because expression of a sequence could be lost during the progression toward metastasis, do not negate the recognition that Applicant's asserted utilities are more likely than not true. Applicant asserts that in some instances a protein may have altered expression in metastatic cancer versus primary cancer, however, this does not compromise the general contention set forth by Applicant that there would be a reasonable expectation that the claimed prostate-specific sequences are useful for the detection of cancer in a patient, in view of the specification, in view of the previously submitted Declaration by Dr. Houghton, and further in view of the general knowledge in this art.

Applicant's arguments set forth in paper No.32 have been considered but are not deemed to be persuasive for the following reasons:

It is noted that the specification, and the Declaration by Dr. Houghton only disclose that the claimed sequences are prostate specific. There is no disclosure or indication that the claimed sequences are detected in serum of prostate cancer patients and not in normal controls, or overexpressed in serum as compared to normal controls.

It is further noted that the claimed polynucleotides are organ specific, i.e. specific to prostate, and thus their utitlities, based solely on prostate specific property, such as

treating or detecting prostate cancer are not specific, and are shared by other unrelated prostate specific molecules.

Applicant has argued that since the claimed sequences are prostate specific, detection of said sequence in the serum would indicate that the primary prostate cancer has become invasive and entered the circulation. However, it is unpredictable that one could detect the claimed sequences in serum of prostate cancer patients and not in normal controls, i.e. in invasive prostate cells that enter the circulation, because gene expression of primary and metastatic cells are different, wherein loss of expression of genes frequently occur during progression toward metastasis, as taught by Kibel et al and Ren et al. Further, although a single protate specific gene, PSA, is detected in the serum of patients with prostate cancer, and not in normal controls, one could not extrapolate to any other prostate specific gene, because expression of different gene sequences are independent and unrelated to the expression of other gene sequences. In addition, MPEP 2164.08(a) teaches that a single means claim which covered every conceivable means for achieving the stated purpose was held nonenabling for the scope of the claims because the specification disclosed at most only those means known to the inventor. *In re Hyatt*, 708 F.2d 712, 714-715, 218 USPQ 195, 197 (Fed. Cir. 1983).Thus based on a single disclosure by the art, Gelmini et al, on expression of a single prostate specific gene, PSA, one could not extrapolate to the expression of the claimed prostate specific sequences, and thus the claims would be non-enabled according to MPEP 2164.08(a).

Thus in view of the teaching of Kibel et al and Ren et al, and MPEP 2164.08(a), one could not predict that the claimed sequences would be useful for detecting primary prostate cancer cells that have become invasive and entered the circulation.

In view of the above, the claimed sequences lack specific and substantial utilities.

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, WRITTEN DESCRIPTION, NEW REJECTION

o/k amended

The instant specification does not contain a written description of the invention in such full, clear, concise, and exact terms or in sufficient detail that one skilled in the art can reasonably conclude that applicant had possession of the claimed invention at the time of filing.

Claims 35-36, 41-46 are rejected under 35 USC 112, first paragraph.

Claims 35-36, 41-46 are drawn to a method for detecting the presence of "a DNA molecule", comprising detecting the DNA sequences that amplifies in the presence of oligonucleotide primers specific for one of the following sequences of SEQ ID NOs:110, 173-175, 177, 223-224.

The specification discloses an isolated cDNA sequence of SEQ ID NO:110, 173-175, 177, 223, or 224.

The specification fails to identify and describe the 5' and 3' regulatory regions and untranslated regions essential to the function of the claimed invention, which are required since the claimed invention currently encompasses the gene. The art indicates that the structures of genes with naturally occurring regulatory elements and

untranslated regions is empirically determined (Harris et al. J. of The Am Society of Nephrology 6:1125-33, 1995; Ahn et al. Nature Genetics 3(4):283-91, 1993; and Cawthon et al. Genomics 9(3):446-60, 1991). Therefore, the structure of these elements is not conventional in the art and skilled in the art would therefore not recognize from the disclosure that applicant was in possession of the genus of nucleic acid, including genes, comprising SEQ ID NO: 110 or fragments thereof.

Thus, only a method for detecting the presence of the polynucleotide sequence of SEQ ID NO:110, 173-175, 177, 223, or 224, comprising detecting the polynucleotide sequences that amplifies in the presence of oligonucleotide primers specific for one of the following sequences of SEQ ID NOs:110, 173-175, 177, 223-224, but not the full breadth of the claims meet the written description provisions of 35 USC 112, first paragraph.

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, ENABLEMENT, NEW REJECTION

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> "The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention."

1. Claims 29-34, 41-46 are rejected under 35 U.S.C. 112, first paragraph.

Specifically, since the claimed invention is not supported by a well established utility for the reasons set forth in the rejection under 35 USC 101 above, one skilled in the art clearly would not know how to use the claimed invention.

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, SCOPE, NEW REJECTION

Withdrawn

Claims 35-36 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for detecting the presence of a DNA molecule comprising SEQ ID NO:110 in "a blood sample", does not reasonably provide enablement for a method for detecting the presence of a DNA molecule comprising SEQ ID NO:110 in "a biological sample". The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 35-36 are drawn to a method for detecting the presence of a DNA molecule comprising SEQ ID NO:110 in "a biological sample" comprising contacting said sample with a at least two oligonucleotide primers specific for the polynucleotide of SEQ ID NO:110 or complements thereof, and wherein the oligonucleotide primers comprises at least about 10 contiguous nucleotides of SEQ ID NO:110.

It is noted that " a biological sample" encompasses any tissue. In other word, the claims encompass a method for detecting the presence of a DNA molecule comprising SEQ ID NO:110 in prostate cancer cells metastasized to different tissues.

In the Declaration by Dr. Raymond Houghton, on 05/09/01, SEQ ID NO:110 or P501S is found in higher quantities in blood samples of prostate cancer patients than in blood samples from normal donors.

One cannot extrapolate from the teaching in the specification and in the Declaration to the claims, because it is unpredictable that one could use the claimed polypeptide for detecting metastasized prostate cells. It is unpredictable that metastasized prostate cells still express the claimed sequence, because expression of a sequence could be lost during the progression toward metastasis. For example, Kibel, AS et al, 2000, J urol, 164(1): 192-6, of record, teach that gene expression in the chromosomal region 12p12-13 is different in primary and metastatic cells, and that inactivation in the chromosome region 12p12-13 occurs prior to metastasis. Ren, C et al, 1998, Cancer Res, 58(6): 1285-90, of record, teach a loss of expression of lysyl oxidase mRNA during progression to metastasis. Gingrich, JR et al, 1996, Cancer res, 56(18): 4096-4102, of record, teach a loss of normal E-cadherin expression as primary tumors become less differentiated and metastasize.

In view of the above, it would be undue experimentation for one of skill in the art to practice the claimed invention.

REJECTION UNDER 35 USC 102, NEW REJECTION

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 23-24, 35-36 are rejected under 35 U.S.C. 102(e) as being anticipated by US 6,130043.

Claims 23-24 are drawn to a method for detecting prostate cancer in a patient, comprising contacting blood or semen obtained from the patient with a at least two oligonucleotide primers specific for the polynucleotide of SEQ ID NO:110 or complements thereof, and wherein the oligonucleotide primers comprises at least about 10 contiguous nucleotides of SEQ ID NO:110. Claims 35-36 are drawn to a method for detecting a DNA molecule comprising SEQ ID NO:110 in a biological sample, comprising contacting said sample with a at least two oligonucleotide primers specific for the polynucleotide of SEQ ID NO:110 or complements thereof, and wherein the

oligonucleotide primers comprises at least about 10 contiguous nucleotides of SEQ ID NO:110.

US 6,130043 teaches a method for detecting prostate disease in a test sample or a target polynucleotide in a test sample, comprising contacting said test sample with at least one prostate specific polynucleotide or complement thereof, wherein prostate specific polynucleotide has at least 50% identity with a polynucleotide selected from the group consisting of SEQ ID NOS: 1-16, and fragments or complements thereof. US 6,130043 teaches that a test sample includes blood, serum, external secretion of genitourinary tract (column 13, 4th paragraph). US 6,130043 further teaches that a polynucleotide specific for a designated sequence comprises contiguous sequences of at least about 10-12 nucleotides (column 9, third paragraph).

Under MPSRCH sequence similarity search, SEQ ID NO:110 in the claimed method is 99% similar to SEQ ID NO:15 or SEQ ID NO:16 taught by US 6,130043 (MPSRCH search report, 2003, us-09-030-606-110.res, pages 5-6, 9-10).

Because the method of the prior art comprises the same method steps as claimed in the instant invention using the same composition, the claimed method is anticipated because the method will inherently lead to the claimed effects. See Ex parte Novitski 26 USPQ 1389 (BPAI 1993).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MINH-TAM DAVIS whose telephone number is 703-305-2008. The examiner can normally be reached on 9:30AM-4:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, ANTHONY CAPUTA can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0916.

SUSAN UNGAR, PH.D
PRIMARY EXAMINER

MINH TAM DAVIS

May 16, 2003